

REMARKS

Claims 1-9 are now in the case.

Claims 1-9 are rejected.

No claim has been allowed.

The Amendments.

Paragraph [0011] of the specification has been amended to correct the spelling of "*Escherichia*" and of "bacterium's". Paragraph [0023] of has been amended to correct the inadvertent omission of two occurrences of "CFU/ml". Support for "CFU/ml" is found further down in the paragraph. The term "pre-weighed" has also been hyphenated. Paragraph [0024] has been amended to correct the spelling of "throughout" and to change "then" to "than".

Independent Claim 1 has been amended to positively recite morphological and functional characteristics of the claimed attenuated strain that distinguish it from the wild-type (non-attenuated) strain of *Flavobacterium columnare*. Support for the added limitations is found in paragraph [0018] and in paragraph [0024]. Claim 4 has been amended to remove the confusing Markush language as related

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to the single claimed deposit strain.

The Rejection of Claims 2 and 4 under 35 U.S.C. §112, First Paragraph.

Claims 2 and 4 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is based on Applicants' failure to fully comply with the requirements for the future availability of the deposit strain NRRL B-30687. Withdrawal of this rejection is respectfully requested.

As pointed out in Paragraph [0009] of the specification, the claimed strain has been deposited under the conditions of the Budapest Treaty in the Agricultural Research Service Culture Collection (NRRL) in Peoria, IL and has been assigned Accession No. B-30687. **UPON THE ISSUANCE OF A PATENT, ALL RESTRICTIONS ON THE AVAILABILITY OF NRRL B-30687 WILL BE IRREVOCABLY REMOVED WITHOUT RESTRICTION OR CONDITION.**

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**The Rejection of Claims 1, 3 and 5-9 under 35 U.S.C. §112,
First Paragraph.**

Claims 1, 3 and 5-9 stand rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an attenuated, ampicillin resistant *Flavobacterium columnare* which is effective for eliciting a protective immune response in fish against virulent strains of *F. columnare* wherein the protective bacterium is strain NRRL B-30687, does not provide enablement for any other attenuated strain of *Flavobacterium* or their use as a vaccine against virulent strains of *Flavobacterium* in fish. The Examiner further takes the position that the specification fails to provide enablement for the prophylactic use of strain NRRL-B 30687 against virulent *Flavobacterium* species other than *F. columnare*. The Examiner states that the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. Withdrawal of this rejection is requested for the reasons that follow.

Independent Claim 1 is clearly limited to attenuated strains of *F. columnare* which are effective for eliciting an immune response in fish, which immune response is

protective against infection by virulent strains of *F. columnare*. Moreover, Claim 1 as now amended is limited to only those attenuated strains of *F. columnare* that are characterized by smooth-edged colonies and have significantly less ability to adhere to skin tissue than the parent, non-attenuated strain. Applicants have shown in the specification that there is a high degree of correlation between both the smooth-edged colony morphology and skin adhesion on the one hand, and the protective immune response on the other hand (see paragraphs [0018] and [0023]. Accordingly, the person of ordinary skill in the art could obtain other strains of *F. columnare* besides the deposit strain by repeating Applicants' protocol of applying progressively higher concentrations of ampicillin, and then selecting for smooth-edged colonies (typically only 3% of the total population), and then finally assaying for skin adhesion as described in the specification. Given that progressive passage on ampicillin will yield a finite number of smooth-edged colonies, and that adhesion deficiency is easily assayed, and that reduced adhesion is correlated with reduced virulence, it would be expected that the skilled artisan could find other suitable strains

having this combination of characteristics without undue experimentation. Although the mechanism of inducing an immune response may be unknown, assaying for protective immunity strains that have passed the aforementioned colony morphology screen and the adhesion deficiency assay would also be within the skill of the ordinary person in the art and would not require undue experimentation. Challenge experiments for assaying protection are clearly set forth in Applicants' disclosure (see paragraphs [0025] and [0026]).

Applicants wish to point out to the Examiner that the mechanism of protection is not necessarily an antigen-antibody response. The protective "immunity" demonstrated in the disclosure was decreased susceptibility to *F. columnare* challenge infection or increased survival in the fish immunized with the attenuated mutant. The results show that convalescent catfish antibody titers, following immersion challenge, were not significantly different. The antibody response and its relationship to protective immunity following immersion mutant vaccination were not determined. The mechanism of protection may simply be that the mutant blocks adherent sites for attachment of virulent

F. columnaris, instead an antibody or cell-mediated immune response. The proteins identified in the patent were not shown to be antigens or responsible for protection against infection challenge. Accordingly, Applicants contend that identification of other strains within the scope of the claims is entirely within the artisan's skill by assaying for decreased susceptibility to *F. columnare* challenge infection or increased survival in fish immunized with the selected attenuated mutant, without necessarily knowing the amino acid profile of the antigens characteristic of the mutant.

The Rejection of Claim 4 under 35 U.S.C. §112, Second Paragraph.

Claim 4 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Withdrawal of this rejection is requested.

This rejection was based upon inappropriate usage of Markush language in regard to a set having a single item. It was Applicants' intention to claim only the deposit

strain in Claim 4, and therefore the language "selected from the group consisting of" has been deleted.

Summary.

Applicants have amended Claim 1 to positively recite the characteristics needed to identify an attenuated strain of *F. columnare* within the metes and bounds of the claim and as clearly enabled by the disclosure. That is, the claims are now limited to only those attenuated strains of *Flavobacterium columnare* that are characterized by:

1. resistance to ampicillin;
2. smooth-edged colonies;
3. significantly less ability to adhere to skin tissue than the parent, non-attenuated strain of *Flavobacterium columnare*; and
4. efficacy for eliciting an immune response in fish which is protective against infection by virulent strains of *Flavobacterium columnare* (regardless of the mechanism).

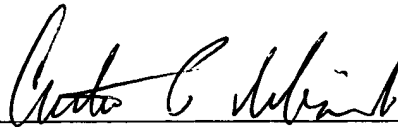
Applicants have also now fully complied with the requirements of 35 U.S.C. §112, first paragraph, in terms of deposits made under the Budapest Treaty.

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The claims are free of the prior art.

Accordingly, Claims 1-9 are deemed to be in condition for allowance, and a favorable action thereon is earnestly solicited.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Curtis P. Ribando", is written over a horizontal line.

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